REMARKS

Applicants have amended claims 16-17 to improve their form and in response to the Examiner's rejection. Claim 18 is canceled.

In particular, applicants have amended claim 16 to recite "c-Jun N-terminal kinase 3" as the definition of JNK3 and to recite a JNK3 mutant molecule, defined as a JNK3 molecule bearing one or more amino acid substitutions, deletions and/or additions. Support for this amendment, which merely clarifies a term in the claim and does not change its scope, can be found throughout the specification as originally filed, for example, on pg. 1, line 32; and pg. 29, lines 17-33.

Applicants have amended claims 16 and 17 to recite the step of determining the atomic coordinates that comprise a binding pocket. Support for this amendment, which does not narrow the scope of the claims, can be found throughout the specification as originally filed on, for example, pg. 9, line 7 to pg. 10, line 2; and pg. 21, lines 18-36.

Applicants have added claim 19, which depends from claims 16 or 17, to recite a further step of contacting the potential agonist or antagonist to a JNK3 or JNK3 mutant molecule to determine its ability to interact

with said JNK3 or JNK3 mutant molecule. Support for this amendment, which does not narrow the scope of the original claim but adds a step to it, can be found throughout the specification as originally filed on, for example, pg. 22, lines 15-33 and Example 6.

Applicants have added dependent claim 20 to add crystallization and X-ray diffraction steps to the methods of claims 16 and 17. Support for this amendment can be found throughout the specification as originally filed at, for example, pg. 6, line 26 to pg. 7, line 36; pg. 27, line 18 to pg. 30, line 20; and Examples 2 and 3.

Applicants have added independent claim 21 to further recite an embodiment of the invention. Support for this amendment can be found throughout the specification as originally filed at, for example, pg. 6, line 26 to pg. 7, line 36; pg. 8, lines 28-30; pg. 21, lines 13-36; pg. 22, line 15-33; pg. 26, lines 1-18; pg. 27, line 18 to pg. 30, line 20; claim 18 as originally filed; and Examples 2, 3 and 6.

None of the amendments adds new matter.

The Objections

Specification

The Examiner has objected to the specification. In particular, the Examiner has objected to the title as not being descriptive since it is directed to a composition, "Crystallizable JNK Complexes", while the elected invention is directed to a method. The Examiner has required an amended title.

Applicants have amended the title to be consistent with the elected claims, thereby obviating the objection.

The Examiner has also objected to applicants' amendment to the specification, in which they previously replaced the paragraph beginning on page 43, line 16, which started with "Figure 1a-5" with a paragraph beginning "Figures 1B-5", stating that said figures do not exist.

Applicants have amended the paragraph to recite Figures 2A, 2B, 3, 4A, 4B, and 5, which are present in the amended drawings or the drawings, as originally filed. This overcomes the rejection.

Sequence Compliance

The Examiner has objected to applicants' amendment to the Sequence Listing. In particular, the Examiner has stated that applicants have not submitted a statement, as required by 37 C.F.R. § 1.821(f), that the

"Sequence Listing" content of the paper or compact disc copy and the compute readable copy are the same.

Applicants traverse.

Applicants submitted Statements in Support of Amendment to Sequence Listing under 37 C.F.R. § 1.825(a) and to Verify Content of Computer Readable Form Submission under 37 C.F.R. §§ 1.821(g) and 1.825(b) with the amended Sequence Listing on September 18, 2003.

Applicants enclose herewith a copy of the aforementioned Statements, as well as a copy of the postcard returned by the PTO confirming receipt of said Statements, as Exhibit A. Therefore, applicants believe they have satisfied the requirement for the filing of a statement confirming that the written and computer-readable forms of the Sequence Listing are identical and respectfully request that the Examiner withdraw this objection.

The Rejections

35 U.S.C. § 112, Second Paragraph: Indefiniteness

Claims 16-18 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject

matter which applicants regard as their invention. In particular, the Examiner states that the use of the abbreviation "JNK3" in claims 16-18 make the claims vague and indefinite if the abbreviation is not accompanied by the full name in parentheses. The Examiner also states that claims 16-18 are also vague and indefinite due to the recitation of "Figure 1", which is no longer in the drawings. Applicants have overcome these rejections by amending the claims.

Applicants have amended claims 16 and 17 (claim 18 is canceled) to recite, in parentheses, "c-Jun N-terminal kinase 3" to define the abbreviation JNK3. Applicants have also amended claims 16 and 17 to recite "Figure 1A." Neither of these amendments changes the scope of the original claims. They do, however, obviate the Examiner's rejection under 35 U.S.C. § 112, second paragraph, and applicants respectfully request its withdrawal.

35 U.S.C. § 112, First Paragraph: Enablement

Claims 16-18 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to enable the claimed method for any molecule comprising a JNK3-like binding pocket other than the crystal structure of JNK3α1. The

Examiner acknowledges that, while applicants have disclosed information that would enable one of skill in the art to make a specific crystal of JNK3α1 for practicing the claimed method, no other protein is so enabled. In particular, the Examiner contends that the method relies on data from an unpredictable art, in this case protein crystallization, which the Examiner alleges to be a trial-and-error method. The Examiner states that this is so because the current technology for producing proteins for the crystallization process is unpredictable, which results in a high failure rate for proteins that are being crystallized. The Examiner, therefore, contends that it would be unreasonable to expect one of skill in the art to use the information disclosed for one specific crystal to make others of predictable quality to practice the claimed method without undue experimentation.

Applicants have amended claim 16 to clarify that the binding pocket is from JNK3 or a JNK3 mutant, which is defined by the atomic coordinates of a set of amino acids according to Figure 1A ± a root mean square deviation. Claim 16, as originally filed and as amended, does not encompass <u>any</u> molecule comprising a <u>JNK3-like binding pocket</u>, but encompasses a specified binding pocket from this particular JNK3 or JNK3 mutant.

The specification enables the full scope of the amended claims (and, in fact, the original claims, which had the very same scope). First, applicants provide guidance as to how one of skill in the art can produce sufficient quantifies of JNK3 or a JNK3 mutant, and modify these proteins to improve their solubility and to obtain diffraction quality crystals. See, for example, page 6, line 26 to page 7, line 2; and Example 1 (page 30, line 26 to page 32, line 15) in the specification as originally filed. Further, Su et al. (cited below), teaches how to make and purify several JNK3 mutants. See Example 1(D) and Example 2 (B) of Su et al..

Second, applicants have provided in the specification a range of crystallization conditions enabling the production of crystals comprising a JNK3 protein (or mutant) and a chemical entity without undue experimentation. See, for example, page 7, line 4-21; and Example 2 (page 32, line 16 to page 33, line 24) in the specification as originally filed.

Following the guidance in the present application, only routine experimentation would be required to produce the crystals. The 2003 Scapin et al. confirms that combining the protein purification protocols and crystallization conditions disclosed in the instant

specification with the knowledge of one skilled in the art at the priority date of this application, results in the crystallization and structure determination of JNK3 in complex with several classes of inhibitors. See "Purification and Crystallization" and "Data Collection and Structure Solution and Refinement" Sections (pp. 710-711) of G. Scapin et al. *Chem. Biol.* 10, 705-712 (2003), submitted herewith as Exhibit B; and page 39, lines 28-35 of the specification. Thus, amended claims 16-17 and added claims 19 and 20 are enabled.

Claims 16-18 stand rejected under 35 U.S.C. 112, first paragraph, for not reasonably enabling a method for identifying both an agonist and an antagonist of a molecule comprising a JNK3-like binding pocket. The Examiner acknowledges that applicants have provided guidance to the skilled artisan for the use of a specific crystal of JNK3α1 for practicing the claimed invention. However, the Examiner contends that the specification does not enable one of skill in the art to identify both an agonist and antagonist of a molecule comprising a JNK3-like binding pocket with the same binding pocket coordinates. The Examiner states that different effectors, agonists and antagonists have different functions as defined by their chemical and biological properties which in turn determine

how these agonists and antagonists interact with JNK3α1. The Examiner queries how such different effectors can be identified by the same method without requiring undue experimentation. Applicants traverse.

Applicants have amended claim 16 (as well as claim 17, which depends therefrom; claim 18 has been canceled) to delete the recitation of a "JNK3-like binding pocket" and recite a "JNK3 mutant molecule". In view of the description of JNK3-like binding pockets, to be found in the specification as originally filed at, for example, pg. 20, line 2 to pg. 22, line 28, this amendment does not narrow the claims, but merely clarifies what applicants regard as their invention. Specifically, the amendment refers to JNK3 mutant molecules that are within 1.5 Å root mean square deviation with respect to the wild-type JNK3 molecule described in Fig. 1A. In view of this amendment, claims 16 and 17 are enabled and applicants request withdrawal of the rejection.

35 U.S.C. § 103(a): Obviousness

Claims 16-18 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Su et al. (US 6,162,613 A) in view of *In re Gulack*, 703 F.2d 1381, 1385, 217 USPQ 401, 404 (Fed. Cir. 1983). The Examiner contends that Su

et al. discloses a method for identifying an inhibitor (agonist or antagonist) of JNK3, comprising the use of X-ray coordinates and contact between JNK3 and inhibitors determined via modeling and binding assays. The Examiner asserts that inhibitors such as pyridinyl-imidazoles are identified. The Examiner states that although the method of Su et al. does not specify the atomic coordinates of JNK3, the specific limitations of the atomic coordinates do not distinguish the instant invention from the prior art because said atomic coordinates are nonfunctional descriptive matter. In particular, the Examiner states that the atomic coordinates of Figure 1 are merely stored so as to be read or outputted by a computer without creating a functional interrelationship, either as part of the stored data or as part of the computing processes performed by the computer. The Examiner asserts that such descriptive material alone does not impart functionality either to the data as so structured or to the computer itself. The Examiner contends that one of skill in the art would have been motivated to use the method disclosed by Su et al. to identify inhibitors of JNK3.

Claim 16, as amended, reflects a step whereby the practitioner determines that all or part of a set of amino acids constitutes a JNK3 or JNK3 mutant molecule binding

pocket of interest for designing or selecting a potential agonist or antagonist. Su et al. does not teach or suggest the determination of the recited set of amino acids of a JNK3 or JNK3 mutant molecule as the binding pocket for identifying JNK3 agonists or antagonists.

In addition, the determination step requires the intervention of the skilled practitioner and is not merely applying new data to the method steps in Su et al. The determination step is inventive because it requires that the skilled artisan apply her expertise interactively with the disclosed JNK3 structure coordinates to determine which specific set of amino acids in the JNK3 or JNK3 mutant molecule best delineate a binding pocket of interest. Furthermore, the specific set of amino acids determined are advantageous for identifying potential JNK3 agonists or antagonists compared to other possible sets of amino acids from a JNK3 or JNK3 mutant molecule that could define the binding pocket.

Thus, claims 16-18 (amended claims 16 and 17 and added claim 19 which depends therefrom; claim 18 is canceled) are not obvious in view of Su et al.. In view the above arguments, applicants request the withdrawal of the rejection under 35 U.S.C. §103.

CONCLUSION

Applicants respectfully request that the Examiner reconsider and withdraw all outstanding objections and rejections, enter the amendments, and pass the resulting claims to allowance.

Respectfully submitted,

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